

# Vein diameter is the major predictor of fistula maturation

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**Objectives:** Preoperative duplex ultrasound mapping of veins and arteries has been widely advocated to maximize the creation of native arteriovenous fistula (AVF) for hemodialysis access, but reliable diameter criteria have not been established. We sought to determine patient and anatomic variables predictive of fistula maturation in patients receiving their initial permanent hemodialysis access.

**Methods:** All patients undergoing dialysis access creation from January 2003 to June 2007 were retrospectively reviewed. We analyzed fistula type and functional maturation rates (Society for Vascular Surgery [SVS] reporting standards) based on patient characteristics and findings on physical examination, preoperative vein mapping studies, or venography. Maturation and patency rates were determined by Kaplan Meier analysis. The following factors were analyzed: age, race, gender, body-mass index (BMI), fistula site, preoperative duplex vein diameter, diabetes, hyperlipidemia, HTN, prior central catheter placement, HIV, and history of IV drug abuse.

**Results:** From January 2003 to June 2007, 298 vascular access procedures were performed. One hundred ninety-five (65%) were initial hemodialysis access procedures, among which a native AVF was created in 185 (95%); 158 patients with posterior radiocephalic AVF (PRCAVF,  $n = 24$ ), wrist radiocephalic AVF (WRCADF,  $n = 72$ ), or brachiocephalic AVF (BCADF,  $n = 62$ ) had adequate follow-up and were included in the analysis. PRCAVF, WRCADF, and BCADF had 54%, 66%, and 81% maturation rates, respectively. Both the type of fistula type ( $P = .032$ ) and vein size ( $P = .002$ ) significantly affected maturation by univariate analysis. In contrast, by multivariate logistic regression analysis, vein diameter was the sole independent predictor of fistula functional maturation ( $P = .002$ ).

**Conclusion:** In this series of 158 patients undergoing initial hemodialysis access creation, native AVF creation was performed in 95%. In contrast to previous reports, age, gender, diabetes, and BMI had no significant effect on functional maturation. By multivariate logistic regression analysis, vein diameter was the sole independent predictor of functional fistula maturation. (J Vasc Surg 2009;49:1499-504.)

The U. S. Renal Data Systems (USRDS 2007) estimated greater than 340,000 patients received hemodialysis in 2005 and estimated an incidence of 317 patients per million in that same year.<sup>1</sup> The rate has continued to rise 2.8% since the year 2000. Native arteriovenous fistula (AVF) is the preferred modality for hemodialysis access due to lower rates of thrombosis, infection, and need for secondary interventions compared to grafts, as well as longer survival and functional patency rates.<sup>2,3</sup> The National Kidney Foundation Kidney Disease Outcome Initiative (NKF K/DOQI)<sup>4</sup> implemented guidelines that resulted in the Centers for Medicare and Medicaid Services (CMS) to help sponsor the Fistula First Breakthrough Initiative (FFBI) (also known as the National Vascular Access Improvement Initiative) to increase native AVF rates to 66% by the year 2009.

The NKF K/DOQI recommends that the first choice for native AVF is a wrist (radiocephalic) fistula, second is an elbow (brachiocephalic) fistula, and third is either a transposed brachial basilic vein fistula or a forearm arteriovenous

graft. Despite the known higher incidence of failed maturation for radiocephalic fistulas,<sup>5</sup> the ease of placement and the preservation of proximal vessels for future access outweigh such disadvantages. In addition to a complete history and physical examination, routine preoperative duplex ultrasonography (DUS) is also recommended by NKF K/DOQI guidelines in all patients planned for hemodialysis access. This has led to the increase of native AVF placement and use.<sup>6-9</sup> However, the role of duplex ultrasound in predicting maturation varies in the literature.

The purpose of this study is to carefully evaluate variables that affect initial autogenous hemodialysis accesses maturation in the era of NKF K/DOQI. In addition, we plan to evaluate the role of preoperative DUS vein sizes in relation to fistula maturation. We suspect that patient factors such as age, gender, presence of diabetes, small vein sizes, and radial-cephalic fistulas would have lower maturation rates and would parallel similar failure rates in the literature.<sup>10,11</sup>

## METHODS

Patients referred for permanent hemodialysis access from January 2003 to July 2007 had their records retrospectively reviewed. Approval from the University of Arizona Institutional Review Board was obtained. The selected populations were all direct referrals to a vascular surgery practice at the University of Arizona Health Sciences Center. All operations were performed at the Univer-

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Competition of interest: none.

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sity Medical Center. Only patients with first time permanent hemodialysis access were included in the analysis. The presence of a temporary dialysis catheter was not an exclusion criterion. Information on patients with initial arteriovenous fistula (AVF) or arteriovenous grafts (AVG) were stored in a secure, Health Insurance Portability and Accountability Act (HIPAA) compliant manner. Demographic data such as age, gender, race, and body-mass index (BMI), in addition to comorbidities such as diabetes, hyperlipidemia, hypertension, tobacco use, human immunodeficiency virus (HIV) status, and history of intravenous drug abuse, were documented. Etiology of renal failure was noted along with the absence or presence of prior central catheter access during fistula placement.

Arterial assessments included pulse examination, segmental blood pressures in both upper extremities, and the Allen test for continuity of the palmar arch. Venous assessments include gross evaluation of the veins in the dependent position with tourniquet enhancement in the upper arm. Vein diameter was not estimated on physical exam. Selection and placement of a permanent hemodialysis access, based on physical examination alone, relies on the assessment of the examining vascular surgeon.

Duplex ultrasonography (DUS) of arteries and veins was an adjunct to physical examination in patients with uncertainty to the quality and anatomy of the targeted vessels. These noninvasive imaging were performed using a 5, 6, or 12 MHz scanning probe (Philips HDI 3000 and 5000 Systems, Amsterdam, The Netherlands) by registered vascular technologists in an accredited vascular laboratory (Intersocietal Commission for the Accreditation of Vascular Laboratories). Vein assessments included diameter, compressibility, depth, and continuity. These findings were documented on a standardized form that has anatomical illustrations to reflect findings at a specific location. Vein sizes were recorded at the wrist, distal forearm, midforearm, proximal forearm, antecubital fossa, distal upper arm, mid upper arm, and proximal upper arm (performed both with and without a forearm and arm tourniquet). The mean, largest, and smallest vein diameter for a given anatomic region (ie, forearm or upper arm) were recorded into the database. Extremity arterial duplex assessment, if performed, included the radial and brachial arterial size, presence or absence of calcification, segmental pressure, and velocity waveforms. If physical examination and duplex ultrasonography failed to demonstrate vessels necessary for access, then venography was performed under protocols developed by the division of interventional radiology.

The choice of operation for native AVF or AVG creation is based on the overall assessment of a board certified vascular surgeon after evaluating all preoperative findings. A uniform size threshold for acceptable vein diameter was not used during the study period. All operations were performed in the operating room under local, regional, and/or general endotracheal anesthesia. All anastomoses were performed using monofilament nonabsorbable polypropylene running sutures. Patients were then seen

**Table I.** Distribution of hemodialysis access procedures

	Number (%)
Total hemodialysis access	298
Prior access procedure	103
First access procedure	195 (100)
Autogenous AV access	185 (95)
PRCAVF (Snuff-box)	31 (16)
WRCAVF (Brescia-Cimino)	78 (40)
BCAVF (Kaufman)	72 (37)
BBAVF	4 (2)
Nonautogenous AV Graft	10 (5)
Lost to follow up	23 (12)

BBAVF, Brachial-basilic arteriovenous fistula; BCAVF, Brachial-cephalic arteriovenous fistula; PRCAVF, Posterior radial-cephalic arteriovenous fistula; WRCAVF, Wrist radial-cephalic arteriovenous fistula.

routinely 7 to 14 days postoperatively and then 4 to 6 weeks thereafter to assess for adequate maturation.

All data were entered into Excel spreadsheet (Microsoft, Redmond, Washington, USA). Data were entered and reported using the Society for Vascular Surgery (SVS) reporting standards for dealing with arteriovenous hemodialysis access.<sup>12</sup> The primary endpoint was fistula *maturation* and fistula *functional maturation*. Fistula *maturation* is defined by the determination of both vascular surgeon and nephrologist that an access is patent and ready for cannulation based on adequacy of blood flow through the fistula and the adequacy of vein dilation with respects to length (>10 cm segment), depth (<6 mm), and diameter (>6 mm).<sup>4</sup> This can be based on physical examination with or without postoperative duplex ultrasound (DUS) evaluation. *Functional maturation* is defined as successful cannulation of the fistula with the ability of the access to deliver a flow rate of 350 to 400 ml/min and maintain dialysis for 4 hours or less.<sup>12</sup> Primary fistula failure is defined as fistula abandonment prior to cannulation regardless of patency status.

**Statistical analysis.** Statistical analysis was performed using SAS Statistics, version 9.2 (Cary, North Carolina, USA).  $\chi^2$  analyses were used for independent variables and value of  $P < .05$  was considered statistically significant. Logistical regression was used to calculate covariates of interest coupled to fistula maturation. Time to maturation and primary patency rates were evaluated with Life Table estimates.

## RESULTS

**Patients.** From January 2003 to July 2007, 298 permanent dialysis access procedures were performed at the University Medical Center by four board certified vascular surgeons. A total of 195 operations were first-time access. Autogenous AV accesses were placed as first time permanent access in 185 (95%) patients. The types of autogenous AV access are listed in Table I with similar numbers for both direct native wrist radiocephalic AVF (WRCAVF) and brachiocephalic AVF (BCAVF). Of the primary autogenous AV fistulas, patients with brachial-basilic arteriovenous fistula

**Table II.** Demographic and clinical data for primary hemodialysis access

Characteristic	Number (%)
Total patients in analysis	158 (100)
Age (y)	
Mean	58 ± 1.29
Range	12-91
>65	59 (37)
Gender	
Male	99 (63)
Female	59 (37)
Ethnicity	
Hispanic	71 (45)
Caucasian	69 (44)
African American	9 (6)
Native American	8 (5)
Comorbidities	
Diabetes mellitus	93 (59)
Hypertension	148 (94)
Tobacco use	26 (16)
Etiology of Renal Failure	
Diabetes mellitus	76 (48)
Hypertension	31 (20)
PCKD	7 (4)
Glomerulonephritis	6 (4)
Other <sup>†</sup>	29 (18)
Unknown	9 (6)
Access based on physical examination only	61 (38)
Preoperative duplex ultrasound scanning	88 (56)
Preoperative venogram	11 (6)
Mean follow-up (days)	
PRCAVF (n = 24)	463 ± 91.7
WRCAVF (n = 72)	468 ± 56.7
BCAVF (n = 62)	476 ± 50.0
Overall (n = 158)	471 ± 35.3

PCKD, Polycystic kidney disease.

<sup>†</sup>Other, acute tubular necrosis (ATN), congestive heart failure (CHF), monoclonal gammopathy of undetermined significance (MGUS), systemic lupus erythematosus (SLE), aminoglycoside toxicity, amyloidosis, cyclosporine toxicity, focal segmental glomerulosclerosis, septicemia, multiple myeloma, nephrectomy for malignancy, post renal obstruction, schistosomiasis, short bowel syndrome.

tulas (n = 4), and patients with no follow up after fistula placement were not included in analysis. Patients with grafts were not included in further analyses. Mean follow up was 15.2 ± 1.5 months.

**Demographics.** Table II summarizes 158 total patients with primary autogenous permanent access with adequate follow up. The mean age was 58 ± 1.29 years, with 37% of patients older than 65 years of age. Male patients comprise a majority of the study group. A total of 80 (51%) patients were already on dialysis with a central venous catheter. Diabetes was defined as adult onset, controlled with diet or insulin, or juvenile onset as described by SVS reporting standards. Similarly, hypertension was considered diastolic blood pressure greater than 90 mm Hg, or blood pressure controlled with one or more anti-hypertensive medications. Since 94% of patients had hypertension, severe hypertension (hypertension requiring two or more antihypertensive medications) was used a covariate of interest. Three patients had history of intravenous

**Table III.** Patient population by procedure type and maturation

Procedure	Number (%)	Number matured (%)	Mean days to maturation
PRCAVF	24 (15)	13 (54%)	64.9 ± 8.58
WRCAVF	72 (46)	48 (66%)	79.3 ± 8.76
BCAVF	62 (39)	50 (81%)	89.9 ± 14.18
P-value		.032	.307

BCAVF, Brachial-cephalic arteriovenous fistula; PRCAVF, Posterior radial-cephalic arteriovenous fistula; WRCAVF, Wrist radial-cephalic arteriovenous fistula.

**Table IV.** Causes for primary fistula failure or abandonment

Cause	Number (%)
Thrombosis	17 (36)
Failure to mature	27 (58)
Immediate post procedure steal syndrome	1 (2)
Death	1 (2)
Renal transplant	1 (2)
Total	47 (100)

(IV) drug use (two patients report current use but on exam could still receive an autogenous access.) No patient had a documented or reported history of human immunodeficiency virus (HIV). The most common etiology for renal failure was diabetes in 76 (48%) of patients. DUS vein mapping was performed preoperatively in 88 patients; arterial DUS was performed preoperatively in only 26 patients. Preoperative venograms were ordered in 11 patients (6%). Of note, only three patients had a venogram performed at the request of the vascular surgeon because of inadequate veins on physical examination and DUS. The majority of venograms (nine patients) were ordered and performed prior to evaluation by a vascular surgeon.

**Operative data and maturation outcome.** Table III describes the distribution of fistula types. Of 158 access procedures, 47 fistulas were deemed not mature and were either not used, or abandoned at last follow up (Table IV). A total of 40 fistulas underwent revision, mostly for failure to mature. Eight of the fistulas in which the vein failed to dilate sufficiently for cannulation underwent revision in attempt to salvage the fistula. The total number of fistulas that matured was 111 (70%). Patients who had preoperative DUS or venography had similar maturation rates compared with those without preoperative studies, 71% (68/96) versus 69% (43/62) (Table 5). Overall mean time to fistula maturation was 82 ± 1.29 days (n = 111), and was not significantly different when analyzed against fistula type (P = .307). The total number of fistulas deemed “mature” that actually become functionally mature at first time cannulation was 101 out of 111 (91%). Mean time from fistula creation to first time cannulation was 147 ± 19.6 days. Of 10 ‘mature’ fistulas that failed to achieve functional patency, five were never used due to death, renal transplant,

**Table V.** Maturation based on physical examination only, preoperative duplex ultrasonographic vein size, and venography

Variable	Procedure	Number of patients	Maturation (%)	P-value
Physical exam only	PRCAVF	61	42 (70)	0.760
	WRCAVF	19	11 (57)	0.474
	BCAVF	30	22 (73)	0.277
	BCAVF	12	9 (75)	0.678
Vein size $\geq$ 4.0 mm	PRCAVF	48	45 (94)	<0.0002
	WRCAVF	2	2	0.135
	WRCAVF	18	15	0.341
	BCAVF	28	28	0.005
Venogram		11	7 (70)	0.618

BCAVF, Brachial-cephalic arteriovenous fistula; PRCAVF, Posterior radial-cephalic arteriovenous fistula; WRCAVF, Wrist radial-cephalic arteriovenous fistula.

**Table VI.** Logistical regression analysis comparing covariates with fistula maturation

Risk factor	P-value	Odds ratio	95% Confidence interval
Age 65-99 years	0.672	0.79	0.263 2.366
Gender	0.254	0.52	0.166 1.605
Diabetes	0.482	1.56	0.447 5.501
Hypertension	0.749	1.36	0.210 8.762
Largest vein size on DUS	0.002	0.15	0.044 0.497
BCAVF	0.170	0.45	0.141 1.413

BCAVF, Brachial-cephalic arteriovenous fistula; DUS, Duplex ultrasonography.

or renal preservation at last follow up; two were ligated for arm edema, two were too deep for cannulation and underwent transposition, and one thrombosed during initial dialysis access. Patients that had central venous catheters had a shorter time to cannulation,  $99 \pm 16.6$  days compared with patients without catheters  $241 \pm 43.2$  days ( $P = .004$ ).

Age, race, gender, body-mass index (BMI), diabetes, hypertension, tobacco use, time to referral, and prior dialysis catheter placement had no effect on fistula maturation by univariate or multivariate analysis. Both the type of fistula type ( $P = .032$ ) and vein size determined by DUS ( $P = .002$ ) significantly affected maturation by univariate analysis. In contrast, vein size by DUS was the only significant variable on multivariate logistic regression analysis (Table VI,  $P = .002$ ). This finding was true when the smallest vein size, mean vein size, and largest vein size for an anatomic region were evaluated by DUS (size  $\geq 4$  mm), but was most significant when the largest vein size in a given anatomic region was used, opposed to using the smallest or mean vein diameter.

## DISCUSSION

Vascular surgeons and nephrologists recognize the significant effect of the National Kidney Foundation K/DOQI guidelines on vascular access in patients with chronic kidney disease (CKD) stage 5. One of the notable successes of these guidelines is an increase in native fistula

placement in many centers. K/DOQI guidelines are embraced by the Centers for Medicare and Medicaid Services (CMS) and the Fistula First Breakthrough Initiative (FFBI), which pushes for native arterial-venous fistula with the goal creation rate of 65% by 2009.<sup>13</sup> We report a 95% native autogenous fistula placement in patients presenting for initial permanent hemodialysis access, and a 70% maturation rate.

Our previous experience was reported in 2003 by Patel et al<sup>14</sup> comparing several years of hemodialysis access operations with historical controls. Comparing current experience with the available reports shows that the mean ages were similar (60.9 years vs. 58 years). The prevalence of diabetes (62% vs. 59%) in the population groups is similar. Hypertension, however, was found in 94% (148/158) of patients in the current study compared with 51% (65/128) as previously reported. This could be partly explained by more aggressive control of hypertension. Interestingly, the more noticeable differences observed were changes in regional demographics in patients with CKD. More men had first time access compared to our previous report (63% vs. 45%). Hispanic patients represented an increase in hemodialysis access placement to 45% (71/158) from 38% (49/128). Native Americans rates remain relatively unchanged with 5% (8/158) versus 3% (4/128). Patel et al had a mean maturation rate of 70 days from fistula creation to cannulation. Currently, our rate from creation to cannulation (functional maturity) was 147 days. This is contrasted to results from the Dialysis Outcomes and Practice Patterns Study (DOPPS) with a reported mean cannulation time of 98 days in the United States.<sup>15</sup> It could be inferred that this difference is due to the success of earlier referral for fistula placement and/or aggressive preservation of residual kidney function as encouraged by K/DOQI guidelines. Our data showed that patients with central venous catheters had a significantly shorter time to cannulation, than patients without central venous catheters. Further studies are needed to elucidate factors leading to such an interesting observation.

A functionally mature AV fistula is clearly defined, and widely accepted as the primary goal, but there is no consensus in defining fistula maturation. Dember et al<sup>16</sup> iden-



tifies functional maturation, in a randomized control trial for the Dialysis Access Consortium, as fistula suitability with two needles to maintain an optimal dialysis flow rates of  $\geq 300$  mL/min during eight of 12 dialysis sessions. NKF K/DOQI glossary has fistula maturation as “the process by which a fistula becomes suitable for cannulation” and focuses on the Rules of Sixes: blood flow greater than 600 mL/min; a diameter greater than 0.6 cm; and a depth of approximately 0.6 cm. SVS reporting standards for hemodialysis access do not define *fistula maturation*, but rather define AV access as “patency” and “functional.” *Functional patency* is defined as the ability of a hemodialysis access to deliver a flow rate of 350 to 400 mL/min without access recirculation to maintain a treatment time of less than four hours.<sup>12</sup> We defined fistula maturation as time from access creation to a time an assessment by a vascular surgeon and nephrologist determine a fistula can be cannulated. We report 91% (101/111) of patients we deemed mature by physical examination and post placement imaging, were cannulated successfully (by SVS criteria). K/DOQI recommends that a fistula should be placed at least six months before initiation of hemodialysis. We predict that to meet these guidelines, more fistulas will be created earlier, and potentially will not be utilized for some generous period of time. These should be excluded from functional patency calculations.

It is endorsed by K/DOQI that preoperative DUS has increased fistula placement rates.<sup>6-9</sup> In our report, we found no improvement in maturation rates when DUS was utilized; we placed 38% native fistulas based on physical examination alone with a maturation rate of 69% compared with 71% in patients with preoperative studies. There are no prospective randomized trials comparing physical examinations alone to preoperative DUS in planning fistula placement. Silva et al<sup>9</sup> had minimum of 2.5 mm for vein size as predictable for fistula success. In our current study, we found that only a size  $\geq 4$  mm significantly predicted maturation. Optimal preoperative vein size by DUS for fistula creation has not been validated to prospective randomized trials. Reporting standards for vein mapping (eg, using smallest, largest, or mean vein diameter in a given anatomic area), have not been established. Peterson et al<sup>17</sup> recently noted that despite routine use of DUS vein mapping, disparities in maturation still existed. The authors noted that female gender, age  $>65$  years, and forearm fistulas were predictive of fistula failure. Similarly, the same institution reported earlier that female gender was predictive of fistula failure.<sup>18</sup> We, however, did not observe female gender as a predictive variable to fistula failure. We also did not find age as a variable predictive of maturation failure and agree with Weale et al<sup>19</sup> that age should not be used solely to select type of fistula to be placed.

Vein size logically seems to be a major predictor of fistula maturation if we solely base functional maturity on flow. As Pouseuille's law dictates, flow (Q) is proportional to the product of change in pressure gradient ( $\Delta P$ ) and the fourth power of the vessel radius (r) divided by the viscosity ( $\eta$ ) of blood ( $Q \propto \Delta P \times r^4 / \eta$ ). Larger veins (radius) mean

larger flow. However, such a simplistic view does not take into account the arterial factors and normal pulsatile blood flow. Furthermore, venous compliance after fistula creation needs to be considered. As Corpataux et al<sup>20</sup> found in WRCAVF, vein luminal size can increase by 86% in one week. However, distensibility (compliance) and not size was reported by van der Linden et al to be predictive of fistula maturation.<sup>21</sup> Studies are still mandated to elucidate specific vein characteristics, (early post-operative flow, vein size, or compliance) to increase fistula suitability for dialysis.

We acknowledge that our study has a number of limitations. This is a retrospective review that relies on available patient information and it is vulnerable to availability and accuracy. It exposes the limitation and inadequate follow up in patients we place on permanent dialysis access. Our group size is limited and only patients with adequate follow up were included in the analysis. Furthermore, our definition of fistula maturation is limited on our clinical assessment after fistula placement.

Our group remains aggressive in attempting to place fistulas in all suitable patients. We do not have a current minimal threshold vein size, but continue to use a combination of preoperative DUS vein mapping and physical exam, and we are now looking more consistently at the arteries. In the current study, we had eight patients with the smallest vein diameter on DUS between 1.5 and 2 mm that went on to mature their fistulas, and three that did not, so we believe that surgeon's judgment remains extremely important. We continue to follow the NKF K/DOQI recommendations and start as distally as possible, especially in younger patients. For patients older than 75, we are more reluctant to perform radiocephalic AVF at the wrist.

## CONCLUSIONS

Our experience shows that vein size is the major predictor for a successful fistula. Contrary to previous reports, we did not show any difference in maturation with other patient variables. While there is an increase in fistula placement using DUS, studies are still mandated to develop an optimal vein mapping protocol to predict vein factors that affect maturation rates, including size criteria.

## AUTHOR CONTRIBUTIONS

Conception and design: DMI

Analysis and interpretation: LSL, DMI, ACG, JLM

Data collection: LSL, DMI, KRG, LC

Writing the article: LSL, DMI, LC, ACG, JLM

Critical revision of the article: DMI, KRG, JLM

Final approval of the article: LSL, DMI, DRG, LC, ACG, JLM

Statistical analysis: DMI, ACG

Obtained funding: N/A

Overall responsibility: DMI

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